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l7 and (antigen or pathogen or nucleic or protein or cells or virus or viral).clm.	38

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USPT	l7 and (antigen or pathogen or nucleic or protein or cells or virus or viral).clm.	38	L10
USPT	l7 and (antigen or pathogen or nucleic or protein or cells or virus or viral)	325	L9
USPT	l7 and (antigen or pathogen or nucleic or protein or cells)	307	L8
USPT	l6 same (supposit$ or pass$)	553	L7
USPT	l5 same polyethylene	7968	L6
USPT	sorbitan	28728	L5
USPT	l1 same polyethylene	224	L4
USPT	('6001392')[PN]	1	L3
USPT	l1.ti,ab,clm.	19	L2
USPT	(supposit$ or base) same (polysorbat$ or poly-sorbat$ or (poly near3 sorbate))	705	L1

An example of anaphylaxis caused by the gelatine contained in MMR- vaccine **and Escre** suppository. **(Ministry of Health and Welfare S).**

WATAYA YASUHIKO (1); SAKAGUCHI MASAHIRO (2); INOUE SAKAE (2); CHIBA SHUNZO (3)
(1) Watayashonika; (2) National Inst. of Health; (3) Sapporo Med. Coll.

Yobo Sesshu no Koka to Fukuhanno no Tsuiseki Chosa oyobi Yobo Sesshu no Shakai, Keizai Koka ni kansuru Kenkyu Hokokusho. Heisei 8nen, 1996, PAGE.363-364
JOURNAL NUMBER: N19962021B
UNIVERSAL DECIMAL CLASSIFICATION: 615.37.03 615.214.03
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication

ABSTRACT: This paper presents a 2-year-and-10 month infant case who manifested anaphylaxis by MMRvaccine and gelatine-including Escre suppository. From a result of serum gelatine unique IgE antibody and clinical course, this disease example was diagnosed as immediate-type allergy induced by gelatine contained in MMR-vaccine and Escre suppository.

DESCRIPTORS: vaccination; virus vaccine; suppository; side effect; anaphylaxis; gelatin; pathological state; clinical trial; human(primates); case report; hydrate; aliphatic aldehyde; aliphatic chlorine compound; sedative hypnotic
BROADER DESCRIPTORS: inoculation; prevention of epidemic; vaccine; immunotherapeutic drug; drug; semi-solid preparation; pharmaceutical preparation; action and effect; immunological reaction; reaction; processed protein; protein; animal protein; test; reporting; action and behavior; solvate; addition compound; compound(chemical); aldehyde; carbonyl compound; aliphatic halogen compound; organohalogene compound; organochlorine compound; psychotropic drug; central nervous system drug ; nervinum; central nervous system depressant
CLASSIFICATION CODE(S): GW22020O; GW03110J

Bacterial vaginitis: protection against infection and secretory immunoglobulin levels in the vagina after immunization therapy with Gynatren.

Ruttgers H

University Women's Hospital, Heidelberg, St. Antonius Women's Hospital, Wuppertal, FRG.

Gynecologic and obstetric investigation (SWITZERLAND) 1988, 26 (3) p240-9, ISSN 0378-7346 Journal Code: FYA

Languages: ENGLISH

Document type: CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL

JOURNAL ANNOUNCEMENT: 8907

Subfile: INDEX MEDICUS

In a prospective, randomized double-blind study the prophylactic effect of the immunotherapeutic agent, Gynatren, against reinfection was investigated in 192 patients with bacterial vaginitis (95 treated with the active preparation versus 97 with placebo). In 30 and 25% of the patients in the two groups, respectively, it was the third or even more frequent infection in a period of 12 months. In a further 46 and 39%, respectively, it was the second infection in the course of a year. All the patients were given local treatment with tetracycline-amphotericin B vaginal **suppositories** and at the same time **vaccinated** with Gynatren or placebo. One month after the start of treatment, 85% of the patients in the active-treatment group and 83% in the placebo group were asymptomatic and free from pathogenic bacteria. After 3 months 78% in the active-treatment group and 60% in the placebo group were free from infection. After 6 months 76 and 40%, and after 12 months 75 and 37% of the women in the active-treatment and placebo groups, respectively, were free from clinical symptoms and pathogenic bacteria. These results correlated with the concentrations of local antibodies (secretory immunoglobulin) detectable in the vaginal secretion.

Tags: Female; Human

Medical Research:

New Vaccines May Ward Off Urinary Tract Infections

Robert F. Service

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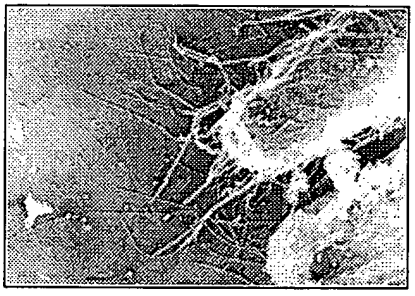
What's almost as common as a cold, but, for most sufferers, far more uncomfortable? Urinary tract infections, or UTIs. Caused primarily by *Escherichia coli*, they send 1.5 million people (mostly women) to the hospital each year in the United States alone, and 7 million more to their doctors. In most cases, the infections are not life threatening: Standard antibiotics usually offer quick relief. But UTIs can recur frequently, and, when untreated, cause kidney damage and even death. A vaccine could reduce this toll, but until now, says Harry Mobley, a microbiologist at the University of Maryland School of Medicine in Baltimore, there has been "little successful work in UTI vaccines."



Bug blocker. A vaccine under development prevents adhesion proteins at the tips of spaghettilike pili on UTI-causing bacteria (above) from latching onto host cells.

S. Hultgren/Washington Univ.

On page 607 of this issue, however, researchers at MedImmune, a Maryland-based biotech company, and at Washington University in St. Louis report that they have developed a genetically engineered, injectable vaccine that prevents UTIs in mice. Meanwhile, researchers at the University of Wisconsin, Madison, are nearing completion of midstage human clinical trials of a vaccine delivered via a vaginal suppository that seems to offer at least short-lived protection. Mobley calls the new studies "very exciting." Not only do they hold out the hope of reducing the number of UTI cases, he says, but the strategy followed by the MedImmune-Washington University group--targeting a single protein that

enables the bacteria to latch onto their target cells--could prove to be valuable against other infections.

These aren't the first efforts to combat UTI-causing microbes. For instance, one injectable cocktail of killed UTI-causing bugs, called Urovac, has been available in Europe since the late 1980s and provides short-lived protection. But natural toxins in the organisms often trigger painful inflammation around the injection site, among other side effects.

To minimize inflammation, the Wisconsin group--led by urologist David Uehling--uses the same concoction of killed organisms as in the Urovac vaccine, but relies on another delivery method: a vaginal suppository. The researchers hoped that by allowing killed microbes to diffuse through the entire vaginal tract instead of injecting them into one small part of a muscle, a suppository would avert inflammation. They reasoned that the killed organisms would still trigger the production of a class of antibodies known as secretory IgA, which circulate in mucosal surfaces such as the lining of the urinary and reproductive tracts and block invading microbes.

In preliminary trials of 25 women, the vaccine seems at least partially effective: Women who are prone to UTIs acquire infections less readily, and none have reported side effects. However, the vaccine's protective effect may diminish over time, says immunologist Walter Hopkins, a member of the Wisconsin team. If that is confirmed in the group's final-stage efficacy trials, says Hopkins, it could mean that women would have to readminister the vaccine, possibly as often as every few months.

The MedImmune-Washington University team, led by MedImmune's Solomon Langermann and Washington University's Scott Hultgren, has adopted what may prove to be an even more promising strategy. Its vaccine triggers the immune system to produce antibodies that block the action of just a single, key protein on UTI-causing microbes. Administering only that protein does away with the need to expose patients to the whole organisms--and their side effect-producing toxins. The researchers targeted an "adhesion" molecule called Filamentous H, or FimH, present on *E. coli*. The microbes deploy FimH on the end of long, spaghettilike strands that extend from the cell body and latch onto sugar molecules on the surface of host cells. Says microbiologist Vince Fischetti of Rockefeller University in New York City, "If you block that interaction, you can prevent infection."

Researchers have tried to develop adhesion vaccines for other diseases such as gonorrhea, which is caused by organisms that rely on adhesion proteins. But in the past, adhesion vaccines "have not panned out very well," says Mobley. When genetically engineered bacteria are coaxed into producing the large amounts of adhesion proteins needed for a vaccine, the proteins often become degraded or clumped together, losing their ability to provoke immune cells into making antibodies targeted to the protein.

So, the MedImmune-Washington University team whipped up two separate vaccine formulations in the hope that at least one would yield suitable proteins. For the first, the researchers genetically engineered *E. coli* to express extra FimH, which they then collected and purified. As in earlier efforts to develop adhesion vaccines, these proteins ended up partially degraded. But fortunately, the part of the protein that triggers a protective antibody response remained intact. In the second formulation, the scientists modified the bacteria to express not only FimH, but also so-called chaperone proteins, which ensure that proteins fold into their proper conformation as they are made.

The team injected separate groups of mice with the two vaccines and exposed them 9 weeks later to UTI-causing *E. coli*. Both groups of vaccinated mice were able to ward off UTIs for more than 7 months, the latest time point studied. Analyses of the animals' urine showed that both vaccines had elicited blood-circulating IgG antibodies, some of which leaked into the mucosal lining of the bladder

and urinary tract. These antibodies, the researchers believe, bound to *E. coli*'s natural FimH proteins, preventing the bacteria from binding to their target cells.

Despite this early success, Mobley and others say that the MedImmune-Washington University team has a long way to go before proving that its adhesion-protein vaccine can make it to market. The researchers will have to demonstrate that the vaccine can block UTI-causing *E. coli* in humans while sparing another colony of *E. coli*: the beneficial intestinal flora that keep disease-producing bugs from proliferating in the gut. Says Mobley: "The current results are still quite preliminary."

In any case, Mobley and others agree, the new adhesion vaccine's initial success could pave the way for developing a host of other such vaccines for other diseases. Adhesion vaccines might just catch on.

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Volume 276, Number 5312, Issue of 25 Apr 1997, p. 533.

▲ PAGE TOP

New vaccines may ward off urinary tract infections.
Service, Robert F
Science (Science) v. 276 (Apr. 25 '97) p. 533
DOCUMENT TYPE: Feature Article
SPECIAL FEATURES: il ISSN: 0036-8075
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
RECORD TYPE: Abstract RECORD STATUS: Corrected or revised record

ABSTRACT: Two new studies have provided promising results in the search for vaccines for urinary tract infections (UTIs). Caused mainly by Escherichia coli, UTIs are responsible for the hospitalization of 1.5 million people each year in the United States alone. In this issue of Science, researchers at MedImmune, a Maryland-based biotech firm, and at Washington University in St. Louis, announce that they have created a genetically engineered, injectable vaccine that prevents UTIs in mice. Researchers at the University of Wisconsin, Madison, meanwhile, have almost finished midstage human clinical trials of a **vaccine** delivered via a vaginal **suppository** that appears to provide at least short-term protection from UTIs.
DESCRIPTORS:
Urinary tract infections--Vaccines and vaccination

dLL`` 00↑↑↑

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USPT	l17 and (composition or vaccin$).clm.	172	L18
USPT	(l3 and l4).clm.	285	L17
USPT	(l4 and l6).clm.	2	L16
USPT	l5 and l6.ti.	45	L15
USPT	l13 not lipid	4	L14
USPT	l12 and (virus or viral or pathogen or microb$ or antigen or protein or dna or nucleic or lipid)	6	L13
USPT	l11 same combin$	11	L12
USPT	l10 same l6	191	L11
USPT	l3 same l4	3460	L10
USPT	l7 and vaccin$.clm. l3 same l4	0	L9
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USPT	(suppositor$ or supositor$)	28569	L6
USPT	(l3 or l4) same (suppositor$ or supositor$)	8149	L5
USPT	polysorbate or poly-sorbate or polysorbat$ or poly-sorbat$	7264	L4
USPT	peg or polyethyleneglycol or poly-ethyleneglycol or polyethylene-glycol or glycol or peg$	226800	L3
USPT	(6001395 or 5672350).pn.	2	L2
USPT	6100066.pn.	1	L1

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L4: Entry 134 of 224 File: USPT Sep 22, 1992

DOCUMENT-IDENTIFIER: US 5149537 A
TITLE: Use of taurocholic acid and its salts as enhancers for calcitonin containing pharmaceutical compositions

BSPR:
For example, UK Patent 1,354,525, dated April 1970, discloses a variety of galenical formulations of fish calcitonin (e.g. salmon calcitonin), including a nebulizer composition, a nasal composition, a sublingual glosset, a topical cream and a suppository composition. A single example is given of a suppository. The suppository base contained lactose, polyethylene glycol 400 and 4,000, polysorbate 80 (polyoxyethylene (20) sorbitan monooleate) and glycerin, and is buffered with lactic acid to pH 4.5. No further details were given of the exact composition.

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?s vaccin? (5n) supposit?		
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	4421	SUPPOSIT?
S1	4	VACCIN? (5N) SUPPOSIT?

?t s1/9/all

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USPT	l26 same polyethylene same l19	0	L34
USPT	l26 same polyethylene same polyglycolic	0	L33
USPT	l26 same polyethylene same polysorbate same polyglyolic	0	L32
USPT	l26 same polyethylene same polysorbate	110	L31
USPT	l29 and polysorbate.clm.	1	L30
USPT	l27 and polyethylene.clm.	21	L29
USPT	l27 and l4.clm.	1	L28
USPT	l26.ti.	85	L27
USPT	supposit$	29920	L26
USPT	5700486.pn.	1	L25
USPT	5,700,586.pn.	1	L24

USPT	5,700,586.pn.	1	L23
USPT	l21 and (supposit$ or pessar$)	4	L22
USPT	l19 same l4	67	L21
USPT	l19 and l4	440	L20
USPT	polyglycolic or poly-glycolic	2432	L19
USPT	l15 same l4	35	L18
USPT	l15 same l3	6	L17
USPT	l15.ti,ab,clm. and ((l3 and l4) or l5 or l6)	3	L16
USPT	suppository near3 base	3246	L15
USPT	l13 and l4	16	L14
USPT	l3 same supposit$	57	L13
USPT	supposit$.clm. and l9	3	L12
USPT	supposit$.ab. and l9	0	L11
USPT	supposit$.ti. and l9	0	L10
USPT	l3 same l4	527	L9
USPT	(l5 or l6) and supposit$.ti,ab.	0	L8
USPT	l5 and supposit$.clm.	3	L7
USPT	l3 near5 l4	146	L6
USPT	l3 near50 l4	279	L5
USPT	peg or peg$ or polyethyleneglycol or polyethylene-glycol or poly-ethyleneglycol or poly-ethylene-glycol	46549	L4
USPT	polyglycol$	19741	L3
USPT	l1 and polyglycol$	1	L2
USPT	4756907.pn.	1	L1

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l8 and bacteria.clm.	28

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USPT	l8 and microbial.clm.	8	L13
USPT	l8 and pathogen.clm.	3	L12
USPT	l8 and immunogen.clm.	0	L11
USPT	l8 and hiv.clm.	12	L10
USPT	l8 and antigen.clm.	7	L9
USPT	(supposit$ or pessar$).clm.	1096	L8
USPT	l6 and (supposit$ or pessar$).clm.	1	L7
USPT	vaccin$ near50 (supposit$ or pessary or rectal or enema or rectum)	140	L6
USPT	supposit$.clm. and vaccin$.clm.	9	L5
USPT	l3 and (vaccin$.clm. or composit$.clm.)	1432	L4
USPT	(rectal or rectum or supposit$ or vaginal or vagina or urogenit$).clm.	3354	L3
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USPT	4873090.pn.	1	L1